REMARKS

Upon entry of the present amendment, claims 1-6, 8-20, 22-34, and 36-106 are pending. Claims 1, 15, and 31 have been amended. Independent claims 1 and 15 were amended to incorporate a claim term (astaxanthin) of dependent claims 7 and 21, which dependent claims have now been canceled. Claim 31 was amended to incorporate a claim term (astaxanthin) of claim 35, which has now been canceled. These amendments are supported by the originally-filed claims and disclosure throughout the specification, e.g., at page 1, line 23, of the specification. Claim 29, and new claims 82, and 101 were amended to recite oral administration; this amendment is supported by disclosure at page 11, line 13, of the specification. Claims 42-102 have been added. New claims 42-53 and 68-83 are supported by the originally-filed claims and the specification at page 2, lines 26-27, of the specification. New claims 54-67 and 84-102 are supported by disclosure throughout the specification, e.g., at page 7, line 8, to page 8, line 17, of the specification. New claims 103 and 104 are supported by disclosure at page 1, lines 23-26, of the specification, and new claims 105-106 are supported by disclosure at page 3, lines 1-2, of the specification.

No new matter has been added by this amendment.

Rejections under 102

Claims 1-4, 7-18, and 21-41 were rejected for anticipation by Gorsek. On page 2, lines 9-12, of the Office Action, the Examiner states:

> Grosek [*sic*] teaches the use of a carotenoid in combination with a polyphenol, a glutathione precursor, a vitamin antioxidant and a lipoic acid in a pharmaceutical composition for the treatment of ophthalmic conditions such a macular degeneration. See abstract, table 1 and claims 1-3.

The claims have been amended to distinguish the claimed invention over the cited art. Claims 7, 21, and 35 have been canceled. Claims 1, 15, and 31 have been amended to require that the carotenoid contain astaxanthin. Table 1 of Gorsek lists Vitamin A but fails to list the specific carotenoid (astaxanthin) now required by the claims. Specifically, Gorsek's formulation is described as containing Vitamin A in the form of 15,000 IU of mixed unspecified "natural carotenoids" and 2,500 IU of specified carotenoids (namely, beta carotene, alpha carotene, lutein, zeaxanthin, cryptoxanthin, and palmitate). Withdrawal of this rejection is respectfully requested.

Rejections under 103

Claims 5, 6, 19, and 20 were rejected for obviousness over Gorsek et al. in view of Kamarei et al. Claims 5 and 6 depend from amended claim 1, and claims 19 and 20 depend from amended claim 15. Independent claims 1 and 15 now require astaxanthin. Since neither Gorsek nor Kamarei describe or suggest astaxanthin, the rejection of claims 5, 6, 19, and 20 should be withdrawn. Originally-filed dependent claims 5 and 19 were rewritten in independent form and added as new independent claim 42 and 68. Thus, the rejection is traversed as it applies to these new claims.

Gorsek's formula is discussed above. Kamarie et al. describe omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) to increase angiogenesis. In support of the rejection, the Examiner states:

> One skilled in the art would have been motivated to combine the teachings of the above references, since one relates to the used of a carotenoid, a polyphenol, a lipoic acid, a vitamin and a glutathione precursor for the treatment of ophthalmic conditions such as macular degeneration which is an angiogenic related disorder and the other relates to the use of EPA and DHA for the treatment of ophthalmic angigenic [*sic*] conditions.

The Examiner is correct in saying that macular degeneration may be an angiogenic disorder. However, contrary to the Examiner's suggestion, macular degeneration is a condition that, in its advanced stages, is characterized by excessive angiongenesis. Dry eye and dry age-related macular degeneration may progress to wet macular degeneration. The distinction is more fully disclosed in the specification at page 18, lines 14-18:

> Macular degeneration is classified as either wet (neovasular) or dry (non-neovasular). About 10% of patients who suffer from macular degeneration have wet AMD. This type occurs when new vessels form to improve the blood supply to oxygen-deprived retinal tissue. However, the new vessels are very delicate and break easily, causing bleeding and damage to surrounding tissue.

Inflammation is an underlying mechanism of dry eye and early-stage dry age-related macular degeneration, which may advance in severity to late-stage or wet macular degeneration (a condition characterized by pathological angiogenesis). Thus, one of skilled in the art would not be motivated to add omega-3 fatty acids of Kamarei to the formulation of Gorsek for macular degeneration, because administering an angiogenic agent to subjects suffering from a condition that in its severe form is characterized by inappropriate or excessive angiogenesis would exacerbate rather than improve the condition. Thus, one of skill in the art would not combine these two references.

Moreover, one of skill in the art would not combine the two references cited by the Examiner, because neither reference deals with an ophthalmic angiogenic condition. Gorsek describes "age related macular degeneration", which means dry (non-neovascular) macular degeneration to one skilled in the art. Kamarei, on the other hand, has nothing whatsoever to do with angiogenic ophthalmic disorders. The only mention of the eye in Kamarei is a rabbit cornea assay - a standard research tool or laboratory assay in which a pellet or wafer containing a

possible angiogenic agent is placed onto the rabbit cornea and growth of new blood vessels measured for the purpose of determining whether or not an agent has angiogenic activity.

In view of the foregoing amendments and clarifications, Applicants submit that the claims as amended are novel and nonobvious over the cited prior art.

CONCLUSION

Applicant submits that the application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

With a three-month extension, these documents are due on or before May 2, 2005. Applicants submit herewith a Petition for a Three-Month Extension of Time, along with the appropriate fee. Thus, Applicants believe no additional fees are due in connection with this filing. However, the Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21534-002CIP.

Respectfully submitted,

/IABeattie/

Ingrid A. Beattie, Reg. No. 42,306
Attorney for Applicant
MINTZ, LEVIN, COHN, FERRIS
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000

Customer No. **30623**